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(74) Agents: **DAVISON, Barry, L.** et al; 2600 Century Square, 1501 Fourth Avenue, Seattle, Wa 98101-1688 (US).

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(71) Applicant (for all designated States except US): **EPIGENOMICS AG** [DE/US]; Kleine Praesidentenstrasse 1, 10178 Berlin (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DAY, Kevin, J.** [US/US]; 27954 251st Avenue SE, Maple Valley, WA 98038 (US). **COTTRELL, Susan** [US/US]; 3509 Meridian Avenue N, Seattle, WA 98103 (US). **DISTLER, Jürgen** [OE/DE]; Hewaldstr. 2, 10825 Berlin (DE). **MOROTTI, Andrew** [US/US]; 316 Bellevue Avenue E., #402, Seattle, WA 98102 (US). **YAMAMURA, Su** [KR/US]; 15349 SE 42nd Street, Bellevue, WA 98006 (US). **DEKKER, Sharon** [US/US]; 23306 SE 209th Place, Maple Valley, WA 98038 (US). **OCAMP, Yreka** [US/US]; 13520 Linden Avenue N, Apt. 425, Seattle, WA 98133 (US). **DEVOS, Theo** [CA/US]; 1208 NE 100th Street, Seattle, WA 98125 (US).

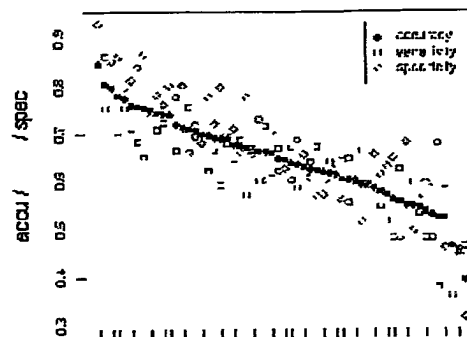
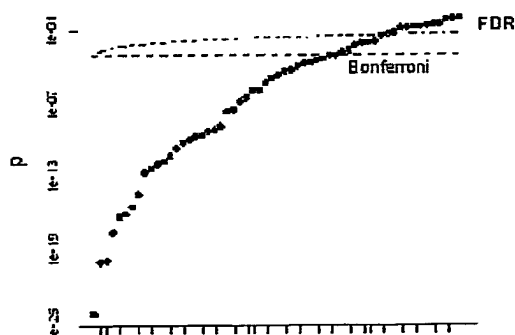
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(54) Title: METHODS AND NUCLEIC ACIDS FOR THE ANALYSIS OF GENE EXPRESSION ASSOCIATED WITH THE DEVELOPMENT OF PROSTATE CELL PROLIFERATIVE DISORDERS



(57) Abstract: The following application provides methods and nucleic acids for the detection of and/or differentiation between prostate cell proliferative disorders. This is achieved by the analysis of the expression status of a panel of genes, or subsets thereof.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER C12Q1/68		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12Q		
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Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal , WPI Data, PAJ, BIOSIS, EMBASE, Sequence Search		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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- / - -		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C		<input checked="" type="checkbox"/> Patent family members are listed in annex
* Special categories of cited documents "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 3 August 2005		Date of mailing of the international search report 20. 12. 2005
Name and mailing address of the ISA European Patent Office P B 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel (+31-70) 340-2040, Tx 31 651 epo nl, Fax (+31-70) 340-3016		Authorized officer Guarinos Vinal s, E

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Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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X	----- DATABASE EMBL human EST 24 May 2000 (2000-05-24), XP002338680 Database accession no. AW853489 abstract	38-41
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2004/040289

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons.

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out specifically
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows.

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers the invention first mentioned in the claims, it is covered by claims Nos. :
2 (completely), 1,4, 5-47 (partially)
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos. :

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest
- ☐ No protest accompanied the payment of additional search fees

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.I

Although claims 5, 14, 33 (that explicitly comprise the step of obtaining from a subject a biological sample) and claim 47 (as far as an "in vivo" method is concerned) are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claim 2 completely and claims 1, 4, 5-47 partially

A method for the detection of and/or differentiation between prostate cell proliferative disorders in a subject comprising contacting genomic DNA isolated from a biological sample obtained from the subject, with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within one or a combination of target nucleic acids, each of said target nucleic acids comprising essentially of all or part of the sequence of the gene or the genomic sequence SEQ ID NO: 1023, a method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject wherein the target sequence comprises, or hybridizes under stringent conditions to at least 16 contiguous nucleotides of a sequence taken from the group consisting of SEQ ID NO: 1023, a method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject wherein distinguishing between methylated and non-methylated CpG dinucleotide sequences within the target sequence (s) comprises methylation state- dependent conversion or non-conversion of at least one CpG dinucleotide sequence to the corresponding converted or non-converted dinucleotide sequence within a sequence selected from the group consisting of SEQ ID NO: 1041 and 1042, a method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject comprising, in each case a contiguous sequence at least 9 nucleotides in length that is complementary to or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 1041 and 1042, a treated nucleic acid derived from SEQ ID NO: 1023, a nucleic acid comprising at least 16 contiguous nucleotides of a treated genomic DNA sequence selected from the group consisting of SEQ ID NOs: 1041, 1042, 1065 and 1066, an oligomer comprising a sequence of at least 9 contiguous nucleotides that is complementary to or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence selected from the group consisting of SEQ ID NO: 1023, a kit comprising bisulfite reagent and an oligomer comprising a sequence of at least 9 contiguous nucleotides that is complementary to or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence selected from the group consisting of SEQ ID NO: 1041, 1042, 1065 and 1066.

Inventions 2-17: claims 1, 3-47 partially

FURTHER INFORMATION CONTINUED FROM POT/ISA/ 210

Inventions 2-17: the same as Invention 1 but relating to SEQ ID NO:57 (GSTP1), SEQ ID NO:20 (PROSTAGLANDIN E2 RECEPTOR), SEQ ID NO:36 (HISTONE H4), SEQ ID NO:1171 (RASSF1A), SEQ ID NO:51 (PR-DOMAIN ZINC FINGER PROTEIN 16), SEQ ID NO:31 (LIM DOMAIN KINASE 1), SEQ ID NO:24 (ORPHAN NUCLEAR RECEPTOR NR5A2), SEQ ID NO:11, SEQ ID NO:1028, SEQ ID NO:4 (LIM/HOMEOBOX PROTEIN LHX9), SEQ ID NO:1116, SEQ ID NO:1025, SEQ ID NO:1020, SEQ ID NO:18 (LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN), SEQ ID NO:1019 and SEQ ID NO:1027 and their respective related sequences as disclosed in Table 26, pages 140-142 of the description.

Invention 18: claims 38-47 partially

A treated nucleic acid derived from SEQ ID NO: 1, a nucleic acid comprising at least 16 contiguous nucleotides of a treated genomic DNA sequence selected from the group consisting of SEQ ID NOS: 60, 61, 178 and 179, an oligomer comprising a sequence of at least 9 contiguous nucleotides that is complementary to or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence of SEQ ID NO: 1, a kit comprising at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence of at least 9 nucleotides that is complementary to or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOS: 60, 61, 178 and 179, their use for the detection of and/or differentiation between or among prostate cell proliferative disorders.

Inventions 19-73: claims 38-47 partially

Inventions 19-73: the same as Invention 18 but relating to SEQ ID NOS: 2, 3, 5-10, 12-17, 19, 21-23, 25-30, 32-35, 37-50, 52-56, 58-1018, 1021, 1022, 1024, 1026 and their respective related sequences as disclosed in Table 26, pages 140-142 of the description.
